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10/537,320	06/02/2005	Akihiro Tada	TOYA107.007APC	3197

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EXAMINER	
SZNAIDMAN, MARCOS L	
ART UNIT	**PAPER NUMBER**
1612	

NOTIFICATION DATE	DELIVERY MODE
01/07/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/537,320	TADA ET AL.	
	Examiner	Art Unit	
	MARCOS SZNAIDMAN	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7,9 and 12-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,9 and 12-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1 page / 09/08/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to applicant's reply filed on October 20, 2009.

Status of Claims

Amendment of claims 7, 9, 12 and 13 and addition of new claims 14-17 is acknowledged.

Claims 7, 9, and 12-17 are currently pending and are the subject of this office action.

Claims 7, 9 and 12-17 are presently under examination.

Priority

The present application is a 371 of PCT/JP03/15267 filed on 11/28/2003, and claims priority to foreign application JAPAN 2002-350733 filed on 12/03/2002.

Should applicant desire to obtain the benefit of foreign priority under 35 U.S.C. 119(a)-(d) prior to declaration of an interference, a certified English translation of the foreign application must be submitted in reply to this action. 37 CFR 41.154(b) and 41.202(e).

Failure to provide a certified translation may result in no benefit being accorded for the non-English application.

Rejections and/or Objections and Response to Arguments

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated (Maintained Rejections and/or Objections) or newly applied (New Rejections and/or Objections, Necessitated by Amendment or New Rejections and/or Objections not Necessitated by Amendment). They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112 (new Rejection Necessitated by Amendment)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9 and 15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 9 and 15 recite the limitation: “wherein the skin has dark complexion on which tyrosine kinase inhibitors have insufficient effect”.

The specification does not provide guidance as to what criteria to apply to determine if the effect is “insufficient”, or as to what particular “effect” is being measured. Accordingly, Applicant has not provided sufficient written description that

would allow the skilled artisan to recognize what type of skins are the ones "on which tyrosine kinase inhibitors have insufficient effect".

Claim Rejections - 35 USC § 112 (New Rejection Necessitated by Amendment)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 9 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9 and 15 are rejected insofar as they recite the term of degree "insufficient effect", which is not adequately defined by the instant specification for the reasons discussed in the written description rejection supra.

Because the term is undefined, it has not been given weight as a limitation for the purposes of applying prior art.

Claim Rejections - 35 USC § 103 (New Rejection Necessitated by Amendment)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

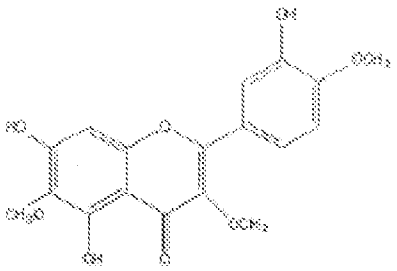
The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

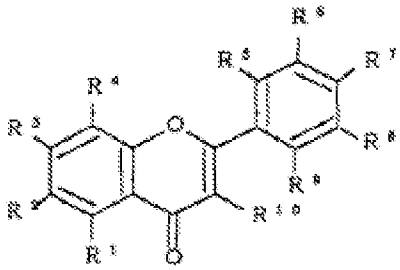
Claims 7, 9 and 12-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ishida et. al. (EP 1147764, cited by applicant, cited in prior office action).

Claims 7 and 9 recite a method for whitening the skin comprising: a step of applying Centaureidin represented by the following formula:



and/or a salty thereof to the skin of an individual in need of skin whitening, whereby elongation of melanocytic dendrites is inhibited.

For claims 7 and 9, Ishida et. al. teach a cosmetic composition of general formula I (see page 3):



, having a sufficient whitening effect, a so called anti skin-aging effect as vitalizing the skin and preventing wrinkles (see page 2, paragraphs [0006] and [0007]). Ishida does not specifically disclose the compound centaureidin. Ishida et. al. limit their structure to at least four methoxy groups (see page 3, line 18), while Centaureidin has three methoxy groups.

However, MPEP 2144, Section III states: prior art structures do not have to be true homologs or isomers to render structurally similar compounds *prima facie* obvious.

In re Payne, 606 F.2d 303, 203 USPQ 245 (CCPA 1979) (Claimed and prior art compounds were both directed to heterocyclic carbamoyloximino compounds having pesticidal activity. The only structural difference between the claimed and prior art was that the ring structures of the claimed compounds had two carbon atoms between two sulfur atoms, whereas the prior art ring structures had either one or three carbon atoms between two sulfur atoms. The court held that although the prior art compounds were not true homologs or isomers of the claimed compounds, the similarity between the chemical structures and properties is sufficiently close that one of ordinary skill in the art would have been motivated to make the claimed compounds in searching for new pesticides). In *re Gyurik*, 201 USPQ 552, 596 F2d 1012 on page 557 states: "In obviousness rejections based on close similarity in chemical structure, the necessary motivation to make a claimed compound, and thus the *prima facie* case of obviousness, rises from the expectation that compounds similar in structure will have similar properties." In this case, it is expected that compounds of general structure I taught by Ishida et. al. and Centaureidin of the instant application, differing by only one –CH3 group, would have similar chemical, physical and biochemical properties.

The phrase: "whereby elongation of melanocytic dendrites is inhibited" is not given any patentable weight because: the whereby clause represents the intended result of the process steps positively recited. See MPEP 2111.04: In *Hoffer v. Microsoft Corp.*, 405 F.3d 1326, 1329, 74 USPQ2d 1481, 1483 (Fed. Cir. 2005), the court held that when a "whereby" clause states a condition that is material to patentability; it cannot be ignored in order to change the substance of the invention." Id.

However, the court noted (quoting Minton v. Nat 'l Ass 'n of Securities Dealers, Inc., 336 F.3d 1373, 1381, 67 USPQ2d 1614, 1620 (Fed. Cir. 2003)) that a "whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited." Id.

Alternatively, even if one were to give some weight to the phrase: "whereby elongation of melanocytic dendrites is inhibited", it does not result in a manipulative difference with the prior art and will necessary be present in the method made obvious by Ishida, since Ishida teaches the same active steps of the instant application: applying Centaureidin to the skin of individuals of skin whitening. In other words, products of identical or similar composition cannot exert mutually exclusive properties when administered under the same circumstances. MPEP 2112 I states: "The discovery of a previously unappreciated property of a prior art composition or a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer".

Since Ishida et. al. teach a method of skin whitening with compounds of formula I (see above), and since centaureidin, which differs from those compounds by just one methyl group is expected to have similar chemical and biological properties, at the time of the invention it would have been *prima facie* obvious for a person of ordinary skill in the art to substitute one functional equivalence (any compound of formula I or structurally related to formula I) for another (centaureidin) with an expectation of success, since the prior art establishes that both function in similar manner, thus resulting in the practice of claims 7 and 9, with a reasonable expectation of success.

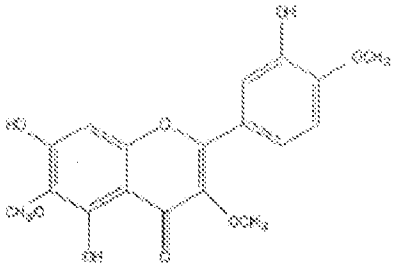
Claim 12 is a narrower version of claim 7, which insofar recites the same limitations as claim 7, wherein a skin preparation for external use comprising 0.005 to 5% by weight of Centaureidin is applied.

Claim 13, further limits claim 12, wherein the skin preparation for external use is a cosmetic.

For claims 12 and 13, Ishida further teaches: that the cosmetic composition (cosmetic compositions are for external use) of the present invention includes 0.00005 to 10% by weight of the compounds of formula I (see page 2, paragraph [0007]). These percentages clearly overlap with the percentages of the instant claims.

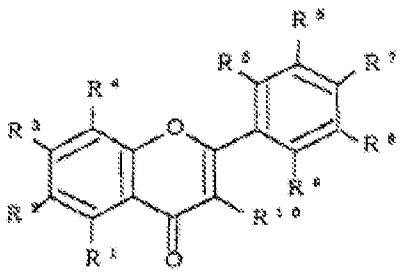
Ishida does not teach the exact same percentages of the instant claims. However, MPEP 2144.05 states: In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. *In re Wertheim,* 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990). Thus resulting in the practice of claims 12-13 with a reasonable expectation of success.

Claims 14-15 recite a method for treating dyschromatosis (a skin disease in which individuals have anomalous skin pigmentation) comprising: a step of applying Centaureidin represented by the following formula:



and/or a salty thereof to the skin of an individual in need of skin whitening, whereby elongation of melanocytic dendrites is inhibited.

For claims 14-15, Ishida et. al. teach a cosmetic composition of general formula I (see page 3):



, having a sufficient whitening effect, a so called anti skin-aging effect as vitalizing the skin and preventing wrinkles (see page 2, paragraphs [0006] and [0007]). Ishida does not specifically disclose the compound centaureidin (Ishida et. al. limit their structure to at least four methoxy groups (see page 3, line 18), while Centaureidin has three methoxy groups) or the specific treatment of dyschromatosis

However, MPEP 2144, Section III states: prior art structures do not have to be true homologs or isomers to render structurally similar compounds *prima facie* obvious. *In re Payne*, 606 F.2d 303, 203 USPQ 245 (CCPA 1979) (Claimed and prior art

compounds were both directed to heterocyclic carbamoyloximino compounds having pesticidal activity. The only structural difference between the claimed and prior art was that the ring structures of the claimed compounds had two carbon atoms between two sulfur atoms, whereas the prior art ring structures had either one or three carbon atoms between two sulfur atoms. The court held that although the prior art compounds were not true homologs or isomers of the claimed compounds, the similarity between the chemical structures and properties is sufficiently close that one of ordinary skill in the art would have been motivated to make the claimed compounds in searching for new pesticides). In *re Gyurik*, 201 USPQ 552, 596 F2d 1012 on page 557 states: "In obviousness rejections based on close similarity in chemical structure, the necessary motivation to make a claimed compound, and thus the *prima facie* case of obviousness, rises from the expectation that compounds similar in structure will have similar properties." In this case, it is expected that compounds of general structure I taught by Ishida et. al. and Centaureidin of the instant application, differing by only one –CH3 group, would have similar chemical, physical and biochemical properties.

The phrase: "whereby elongation of melanocytic dendrites is inhibited" is not given any patentable weight because: the whereby clause represents the intended result of the process steps positively recited. See MPEP 2111.04: In *Hoffer v. Microsoft Corp.*, 405 F.3d 1326, 1329, 74 USPQ2d 1481, 1483 (Fed. Cir. 2005), the court held that when a "whereby" clause states a condition that is material to patentability; it cannot be ignored in order to change the substance of the invention." Id. However, the court noted (quoting Minton v. Nat 'l Ass 'n of Securities Dealers, Inc., 336

F.3d 1373, 1381, 67 USPQ2d 1614, 1620 (Fed. Cir. 2003)) that a "whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited." Id.

Alternatively, even if one were to give some weight to the phrase: "whereby elongation of melanocytic dendrites is inhibited", it does not result in a manipulative difference with the prior art and will necessary be present in the method made obvious by Ishida, since Ishida teaches the same active steps of the instant application: applying Centaureidin to the skin of individuals of skin whitening. In other words, products of identical or similar composition cannot exert mutually exclusive properties when administered under the same circumstances. MPEP 2112 I states: "The discovery of a previously unappreciated property of a prior art composition or a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer".

Since Ishida et. al. teach a method of skin whitening with compounds of formula I (see above), and since dyschromatosis is a diseases associated with anomalous darkening of the skin, and since centaureidin, which differs from those compounds by just one methyl group is expected to have similar chemical and biological properties t, at the time of the invention it would have been *prima facie* obvious for a person of ordinary skill in the art to substitute one functional equivalence (any compound of formula I or structurally related to formula I) for another (centaureidin) with an expectation of success, since the prior art establishes that both function in similar manner, thus resulting in the practice of claims 14-15, with a reasonable expectation of success.

Claim 16 is a narrower version of claim 14, which insofar recites the same limitations as claim 14, wherein a skin preparation for external use comprising 0.005 to 5% by weight of Centaureidin is applied.

Claim 17, further limits claim 16, wherein the skin preparation for external use is a cosmetic.

For claims 16 and 17, Ishida further teaches: that the cosmetic composition (cosmetic compositions are for external use) of the present invention includes 0.00005 to 10% by weight of the compounds of formula I (see page 2, paragraph [0007]). These percentages clearly overlap with the percentages of the instant claims.

Ishida does not teach the exact same percentages of the instant claims. However, MPEP 2144.05 states: In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. *In re Wertheim,* 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990). Thus resulting in the practice of claims 16-17 with a reasonable expectation of success.

Response to Applicant's arguments related to the above rejection

In a previous response, Applicant argued that the compounds of Ishida, despite the structural similarities with centaureidin, differ from centaureidin in their mechanism of action: centaureidin, inhibits elongation of melanocytic dendrites and has negligible

effect on melanin production, while the compounds disclosed by Ishida have the opposite effect: inhibit melanin production and have no effect on melanocytes elongation (see for example response by Applicant and 1.132 declaration dated 04/22/09), and as such will show different therapeutic effects. However, the specification provides data that shows that Centaureidin is effective in treating the same disease as the compounds disclosed by Ishida: skin whitening (see examples 2 through 4 on pages 16-20 of the specification). For example on page 16, Example 2 describes the patients being treated as: "twenty persons in total suffering from dark complexion that was not alleviated by usual cosmetics inhibiting the production of melanin were used to examine the degree of alleviation of dark complexion". However, Applicant has not provided any specific information regarding who these individuals are (having dark complexion that was not alleviated by usual cosmetics inhibiting the production of melanin, see also 112 2nd rejection). There is no mention of the treatment of individuals with dyschromatosis either with the compounds disclosed by Ishida or with centaureidin. As such, Applicant has not provided any unexpected result for centaureidin, when compared to the compounds of Ishida, except for the different mechanism of action.

Withdrawn Rejections and/or Objections

Claims rejected under 35 USC 112, second paragraph.

Due to applicant's amendment of claims 7-9 and 12-13, the 35 USC 112, second paragraph rejection is now moot.

Rejection under 35 USC 112, second paragraph is withdrawn.

Claims rejected under 35 USC 102(b)

Due to applicant's amendment of claims 7-9 and 12-13, the 102(b) rejection is now moot.

Rejection under 35 USC 102(b) is withdrawn.

Claims rejected under 35 USC 103(a)

Due to applicant's amendment of claims 7-9 and 12-13, the 103(a) rejection is now moot.

Rejection under 35 USC 103(a) is withdrawn.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCOS SZNAIDMAN whose telephone number is (571)270-3498. The examiner can normally be reached on Monday through Thursday 8 AM to 6 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached on 571 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MARCOS SZNAIDMAN/
Examiner, Art Unit 1612
December 19, 2009

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612